2.0 NON-TECHNICAL ABSTRACT

Ovarian cancer is the fourth most common cause of cancer death among women in the United States. Approximately one in seventy women will develop ovarian cancer in her lifetime. If diagnosed early and treated before the cancer has spread, 90% of women will live for more than five years. However, most women are diagnosed with advanced stages of disease. Overall, only 42% of women diagnosed with ovarian cancer will live for more than five years. Clearly, new therapies are needed.

A gene called E1A may be able to stop the growth of cancer by making the tumor cells die or making them more sensitive to other cancer treatments like chemotherapy or radiation therapy. The E1A gene is obtained from a small part of the DNA of a common cold virus. It can be introduced into tumor cells by combining it with some lipid or fat, and then injecting it directly into tumors or into body cavities where tumors might be present. In this case, the combination is called tgDCC-E1A. tgDCC-E1A has been given to mice in experimental models of ovarian cancer with and without chemotherapy. It has been shown to be safe, to make the tumors smaller, and to help the mice with cancer live longer.

tgDCC-E1A has been given via infusion into the abdomen to over 40 women with ovarian cancer. The first studies were conducted using tgDCC-E1A alone. Side effects consisting of nausea, vomiting, abdominal pain, and fever developed in patients treated at the highest doses. A more recent study has been conducted using tgDCC-E1A in combination with a certain chemotherapy regimen which combined paclitaxel delivered intravenously and cisplatin delivered by infusion into the abdomen. In that study, subjects tolerated higher doses of tgDCC-E1A. Some symptoms of nausea, vomiting and abdominal pain were seen, but have not been as severe.

Ovarian cancer patients who develop recurrent disease less than six months after treatment are considered to have "platinum-resistant" disease. These patients are treated with a variety of chemotherapy drugs with marginal success. The efficacy of these regimens might be improved with addition of tgDCC-E1A.

To explore possible improvements in treatment for these patients, Targeted Genetics Corporation would like to study tgDCC-E1A in combination with paclitaxel. In this study, up to 30 women with recurrent, platinum-resistant ovarian cancer will receive an infusion of tgDCC-E1A into the abdomen and an infusion of paclitaxel into the vein weekly for six

weeks. For comparison, six subjects will receive an infusion of paclitaxel alone into the vein weekly for six weeks. Subjects who do not have progression of their disease during this time will be treated with an additional six weeks of the same treatment. Subjects will be carefully monitored for safety. To determine the optimal dose combination of tgDCC-E1A and paclitaxel, groups of three study subjects each will be treated at one of four dose combinations. Determination of the highest safe dose combination will allow larger studies to be conducted to determine if tgDCC-E1A plus paclitaxel is effective in treating women with ovarian cancer.